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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/163,272	09/29/1998	JONATHAN DINSMORE	DNI-041CPA	9801

7590

04/24/2003

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EXAMINER

FALK, ANNE MARIE

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 04/24/2003

2915

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/163,272

Applicant(s)

DINSMORE, JONATHAN

Examiner

Anne-Marie Falk, Ph.D.

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 January 2003.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-8,10-18,20-26 and 28-48 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-8,10-18, 20-26 and 28-48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 September 1998 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

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### DETAILED ACTION

The response filed January 21, 2003 (Paper No. 28) has been entered.

Claims 1, 3-8, 10-18, 20-26, and 28-48 remain pending in the instant application.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous Office Action are hereby withdrawn.

#### *Drawings*

The draftsman has objected to the drawings. See the PTO-948 attached to the Office Action of Paper No. 6 (mailed 12/7/99). Applicant may not request that any objection to the drawings be held in abeyance. See 37 CFR 1.85(a).

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-8, 10-18, 20-26, and 28-48 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record advanced on pages 3-9 of the Office Action of Paper No. 6 (mailed 12/7/99), on pages 2-3 of the Office Action of Paper No. 11 (mailed 10/18/00), on pages 2-3 of the Office Action of Paper No. 14 (mailed 7/3/01), and on pages 2-4 of the Office Action of Paper No. 25 (mailed 7/16/02), because the specification, while being enabling for a method of treating a xenogeneic subject having spinal cord damage arising from amyotrophic lateral sclerosis or spinal cord injury, does not reasonably provide enablement for treating a xenogeneic subject having spinal cord damage arising from the claim-

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designated neurodegenerative disorders or aging. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1, 3-8, 10-17, 38-42, 45, 47, and 48 are directed to compositions. However, the claims recite an intended use. As such the specification must provide an enabling disclosure for the intended use. Moreover, the intended use must be enabled for its full scope.

The specification fails to provide an enabling disclosure for the method of cell-based therapy because methods of xenotransplantation of neural tissue are not routinely successful and the specification does not offer adequate specific guidance to enable one skilled in the art to practice the claimed invention over the full scope to derive a therapeutic benefit in an immunocompetent diseased animal. The art demonstrates that methods of xenotransplantation of neural tissue is unpredictable due to the immune response of the host, which leads to graft rejection if adequate immunosuppression cannot be achieved. Brevig et al. (2000) teaches that “in animal models, neural tissue transplanted between species is usually promptly rejected, even when implanted in the brain. Some of the immunological mechanisms that underlie neural xenograft rejection have recently been elucidated, but others remain to be determined and controlled before individuals with neurological disorders can benefit from xenotransplantation” (see abstract). The reference further teaches that “[c]yclosporin, an immunosuppressant that effectively inhibits T-cell alloreactivity, is inadequate at protecting neural xenografts from immune attack in rats” (p. 341, column 2, paragraph 3) and that an “individual with Parkinson’s disease who received porcine embryonic VM grafts about eight months earlier almost completely rejected his grafts, as determined by histology at autopsy” (p. 342, column 1, paragraph 1). The authors suggest that immunosuppression must be more aggressive “or supplemented with another strategy that inhibits or prevents the host T-cell response” (p. 342, column 1, paragraph 1). Although the instant specification suggests masking MHC class-I antigens, there is no teaching that this additional treatment of the donor tissue is sufficient to

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prevent graft rejection. Brevig et al. discuss the trial in Parkinson's patients where porcine embryonic cells were transplanted and points out that graft survival was poor and T cell infiltration was observed in the one subject that underwent autopsy. The authors state "[t]he two strategies to reduce T-cell mediated rejection, masking of MHC class-I antigens and treatment with cyclosporin, were known to be inadequate in the pig-to-rat model. This initial trial has shown that these strategies are also inadequate in humans" (p. 343, column 1, paragraph 1).

Armstrong et al. (2001) provide a detailed discussion of rejection mechanisms for porcine neural xenografts in the immunocompetent rat. In addition to the T cell response, the reference also discusses the humoral response and points out that "[t]he blood-brain barrier (BBB) is normally an effective barrier to the passage of immunoglobulins ... but is compromised by the necessary trauma of the grafting procedure thus allowing transient access of systemically produced antibodies" (p. 213, column 1, paragraph 2). Armstrong et al. detected IgM in rejecting grafts at all time points and therefore point out that the BBB may be compromised for extended periods (p. 213, bottom of column 1 to top of column 2).

Larsson et al. (2000) report some functional recovery in rats xenografted with porcine embryonic ventral mesencephalic tissue, but point out that graft rejection remains as a significant issue and that more effective immunosuppressive drug treatments are needed.. The reference reports that "[i]mmunosuppressive treatment was necessary for long-term graft survival and functional recovery, but did not sufficiently protect from rejection mechanisms" (see abstract).

Rowe (1996) and Dorling et al. (1997) provide additional discussion of the challenges of xenotransplantation just prior to the effective filing date of the instant application, particularly with regard to hyperacute rejection (HAR) and the further barriers that might exist to limit the survival of xenografts beyond the HAR phase (see abstract of Dorling et al.).

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The Declaration of Dr. Dinsmore has been fully considered but has not been found persuasive because the description of the transplantation procedure is incomplete and therefore it is impossible to know if the transplantations were carried out in accordance with the teachings of the specification.

Given the lack of specific guidance in the specification directed to the wide variety of disorders recited in the claims, the broad scope of the claims, and the limited working examples directed to producing a therapeutic effect upon transplantation of porcine spinal cord cells into an animal model of ALS and an animal model of spinal cord injury, one of skill in the art would have been required to engage in undue experimentation to practice the claimed method over the full scope and use the claimed compositions for their intended use, over the full scope.

*Conclusion*

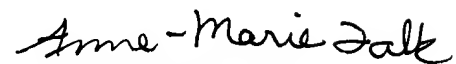
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk, Ph.D. whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, William Phillips, whose telephone number is (703) 305-3482.

Anne-Marie Falk, Ph.D.

  
ANNE-MARIE FALK, PH.D.  
PRIMARY EXAMINER